

## REMARKS

### **I. Status of the Claims**

Claims 13-50 are pending in the application, claims 1-12 having been previously canceled. The claims stand rejected for alleged lack of enablement under 35 U.S.C. §112, first paragraph, and alleged lack of novelty and obviousness under 35 U.S.C. §§102 and 103, respectively. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

### **II. Rejection Under 35 U.S.C. §112, First Paragraph**

Claims 13-24 are rejected as lacking an enabling disclosure under §112, first paragraph. The examiner states that while arguably providing support for the treatment of cancer, the specification lacks adequate support for preventing cancer or events such as tumorigenesis, cell proliferation or metastasis. Applicants traverse.

At the outset, applicants wish to point out that the claims recite "prevent metastasis," not preventing cancer or any other event. Thus, applicants are totally perplexed by the examiner's comments regarding the distinction between preventing metastasis and "prevention of cancer and/or the prevention of cell proliferation," which is nowhere mentioned in the rejected claims. As such, it appears the examiner is rejecting embodiments of the invention which do not exist, and on this basis alone, the rejection is improper.

Turning to applicants' disclosure, applicants submit that the specification does indeed support the use of hyaluronan to prevent metastasis, as discussed in Example 4 and shown in FIG. 6, mice treated with the claimed HA therapy showed a significant reduction in non-lymphoic metastasis, as compared to mice not receiving the therapy. The examiner fails to

discuss these data under (g) of the Wands factors, and therefore applicants consider the Wands analysis provided to be flawed. Thus, the rejection is again improper.

In light of the preceding discussion and evidentiary submission, applicants respectfully request reconsideration and withdrawal of the rejection.

### III. Rejections Under 35 U.S.C. §102

#### A. *Sakurai et al.*

Claims 13-19, 23-30, 34 and 35 stand rejected as anticipated by Sakurai *et al.* The examiner argues that Sakurai teach that hyaluronan and derivatives thereof are effective at drastically reducing breast cancer metastasis in mice. Applicants traverse.

With regard to claims 13-19, 23 and 24, applicants submit that the Sakurai disclose does not provide a teaching of a method in which metastasis is prevented. At most, Sakurai *suggests* such a method. However, the working examples of the reference do not support this methodology, as the data provided indicate that HA will inhibit binding of cells to tissue, *thereby rendering them achorage independent*. As such, this would likely *promote* metastasis, not inhibit it.

Further, with regard to claims 25-30, 34 and 35, these methods all recite combination therapies comprising administration of HA and a chemotherapeutic agent. Sakurai does not disclose *any* combination therapies. Therefore, it cannot anticipate claims that affirmatively recite such combinations.

In light of the foregoing, applicants respectfully submit that the rejections are improper, and request their reconsideration and withdrawal.

**B. *Falk et al. (Application)***

Claims 13-19, 23-30, 34 and 35 stand rejected as anticipated by Falk *et al.* (Application). It is argued that the reference teaches that co-administration of anti-cancer agents and sodium hyaluronate to a patient with breast cancer was effective at treating the cancer and preventing or reducing metastasis. Applicants traverse, but in the interest of advancing the prosecution, claims 13 and 25 have been amended to recite a hyaluronan of 750,000 daltons, which is not taught in the reference. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

**C. *Falk et al. ("the '135 patent")***

Claims 36-49 stand rejected as anticipated by Falk *et al.* ("the '135 patent"). The '135 patent is said to teach that the administration of antineoplastic agents in combination with hyaluronic was effective in achieving total regression of tumors with lack of metastasis. Claim 36 has been amended to recite a hyaluronan of 750,000 daltons. This limitation is not taught in the '135 patent. Furthermore, there is no teaching in the '135 patent regarding the treatment of resistant disease, as claimed. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

**IV. Rejection Under 35 U.S.C. §103**

Claims 20, 21, 30, 31 and 50 stand rejected as obvious over Harper *et al.* in view of Falk *et al.* ("the '834 patent"). Harper is said to teach topical compositions of hyaluronic acid to effect transfer of drugs across the dermal barrier. The '834 patent is cited as teaching the combination of an antineoplastic agent mixed with hyaluronic acid for the treatment of

carcinoma of the bladder with pelvic metastasis. It also is said to teach HA delivery before or after the antineoplastic agent. Thus, the examiner concludes that one of skill in the art would have been motivated to combine HA with an antineoplastic agent for the purpose of improved bioavailability in the treatment of cancer. Applicants traverse.

Claim 50 has been canceled. With regard to the remaining claims, applicants suggest that the references are not combinable as argued by the examiner, as the '088 patent merely employs HA as an inert, carrier molecule, and the '834 patent uses it as a therapeutic. Thus, there would be no reason to combine the two references as they use HA for entirely different purposes.

Second, to the extent that the references do both teach administration of HA, they teach or prefer combination therapy comprising simultaneous or consecutive administration of HA with another agent – by necessity in the '088 patent (since HA is used as a carrier), and by preference in the '834 patent (col. 10, line 49). Thus, claims 20 and 21 which recite a monotherapy are not suggested by the reference.

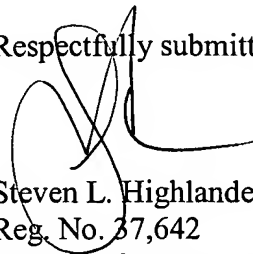
Finally, with regard to claims 20, 21, 30 and 31, which depend from claim 13 and 25, both the '088 and '834 patents suggests use of HA of less than 750,000 daltons, which is inconsistent with the claims as amended (col. 19 and col. 17, respectively). This provides yet another reason that the present invention is distinct.

For all of the foregoing reason, applicants respectfully submit that the claimed invention is distinct from that described in the prior art. Reconsideration and withdrawal of the rejection is therefore requested.

V. **Conclusion**

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding the content of this preliminary amendment, a telephone call to the undersigned is invited.

Respectfully submitted,



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Date: 2/17/04